

REMARKS

The Office Action of March 23, 2004 presents the examination of claims 1-10, 14, and 15. Claims 1-6 and 9-10 are amended. Support for subject matter added to claims 1 and 3 is found in the specification, such as on pages 15-17. Claims 4, 5, 6, 9, and 10 are amended to be dependent on either claims 1 or 3. Claims 16-20 are added. Support for claim 16 is found in original claim 2; support for claims 17 and 18 is found on pages 15-17 of the specification; and support for claims 19 and 20 is found in Tables 1-2 (pages 18-19 of the specification), respectively. Claims 8 and 14-15 are canceled. No new matter is added to the application.

Interview

Applicants' representative extends gratitude to the Examiner and Supervisory Examiner for the interview held on August 3, 2004. In the Interview Summary, the Examiner writes, "Scope of claims in light of teachings of Vogelstein et al. was discussed." Applicants respectfully submit that the claim amendments and remarks presented herein provide a full response to the issues discussed during the interview, and clearly demonstrate that the present invention, as defined in the claims, is neither anticipated nor rendered obvious by Vogelstein et al. Further,

the claims as amended are supported by the specification such that the requirements of 35 U.S.C. § 112, first paragraph are met. Therefore, Applicants respectfully request that the Examiner withdraw all rejections of record, and issue a Notice of Allowance indicating that claims 1-7, 9-10, and 16-20 are allowed.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner maintains the rejection of claim 3 under 35 U.S.C. § 112, first paragraph for allegedly containing new matter. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

During the Interview, the Examiner indicated that she interpreted the phrase "wherein a frameshift or nonsense mutation in a conserved region II and V of p53 is indicative of poor patient outcome whereas a missense mutation in a conserved region III and IV is indicative of positive patient outcome" as a comparison of the severity of mutations in regions II and V with the severity of mutations in regions III and IV. The Examiner asserted that the specification did not show a comparison between

the severity of mutations in regions II and V and the severity of mutations in regions III and IV.

Applicants respectfully clarify that the specification discloses a comparison of mutations within the conserved regions of p53 with mutations outside the conserved regions. See, for example, pages 16-17 and Figures 9-12 of the specification. As shown therein, patients with a p53 mutation in conserved regions II and IV had a much poorer prognosis than patients with a mutation outside the conserved regions. On the other hand, there was no significant difference in the survival rate of patients with a mutation in conserved regions III or IV versus that of patients with a mutation outside the conserved regions of p53.

Thus, the language of claim 3 describing that a frameshift or nonsense mutation in a conserved region II and V of p53 is indicative of poor patient outcome whereas, on the other hand, a missense mutation in a conserved region III and IV is indicative of positive patient outcome, is supported in the specification when each survival rate is compared with that of a patient with a mutation outside one of the conserved regions of p53.

In any event, in order to more closely intimate the language of the specification, claim 3 is amended herein to recite that a mutation in conserved region II or conserved region V of p53 is

indicative of poor patient outcome in comparison with a patient having a mutation outside the conserved regions I-V of p53, and that a mutation in conserved region III or conserved region IV is indicative of positive patient outcome in comparison with a patient having a mutation outside the conserved regions I-V of p53.

Applicants respectfully submit that the subject matter of claim 3 is fully supported by the specification and as such contains no new matter. Withdrawal of the instant rejection is therefore respectfully requested.

Rejection under 35 U.S.C. § 102

The Examiner maintains the rejection of claim 15 under 35 U.S.C. § 102(e) for allegedly being anticipated by Vogelstein '676 (USP 5,527,676). Claim 15 is canceled, thus rendering the rejection moot.

Rejection under 35 U.S.C. § 103

The Examiner maintains the rejection of claims 1, 2, 4-10, and 14 under 35 U.S.C. § 103(a) for allegedly being obvious over Vogelstein '676, in view of Elledge et al. and Callahan et al., and further Hedrum et al. Claims 8 and 14 are canceled, thus

rendering rejection thereof moot. Applicants respectfully traverse the rejection applied to the pending claims. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

During the interview, the Examiner argued that the claims do not distinguish the present invention from Vogelstein et al. In response to the Examiner's remarks, the claims are amended so that they more specifically reflect the data shown in the specification.

In particular, claim 1 is amended to recite that the survival rate following adjuvant therapy of node negative patients without a mutation in p53 is not statistically significant, whereas the survival rate following adjuvant therapy of node negative patients having a mutation in p53 is significantly improved, and the survival rate following adjuvant therapy of node positive patients without a mutation in p53 is not statistically significant, whereas the survival rate following adjuvant therapy of node positive patients having a mutation in p53 is significantly improved.

Claim 3 is amended to recite that a mutation in conserved region II or conserved region V of p53 is indicative of poor patient outcome in comparison with a patient having a mutation

outside the conserved regions I-V of p53, and that a mutation in conserved region III or conserved region IV is indicative of positive patient outcome in comparison with a patient having a mutation outside the conserved regions I-V of p53.

None of the prior art reference disclose the data provided in the specification and reflected in the amended claims. In particular, Vogelstein '676 fails to disclose or suggest the prognostication of the development of neoplasia wherein the metastatic potential of the neoplasia is determined based upon the presence and position of mutation(s). Nor does Vogelstein '676 suggest that certain mutations in p53 are indicative of poor patient outcome. Instead, Vogelstein '676 merely provides the skilled artisan with methods for assessing p53 in human tumors.

As such, Vogelstein '676 fails to anticipate or render obvious the present invention. Further, Elledge et al. and Callahan et al. only teach the general relationship between p53 mutations and breast cancer, whereas Hedrum et al. merely teaches the sequencing of exons 4-9 of p53. Thus, absolutely no reference teaches the inventive methods as claimed in the present application, either alone or in combination.

As such, the present invention is not unpatentable over the combination of references cited by the Examiner. Withdrawal of the instant rejection is therefore respectfully requested.

Claims 17-20

During the Interview, the Examiner suggested adding new claims directed to the data provided in the figures. Claims 17-20 are directed to the mutations described in Tables 1 and 2, and in Figures 13-15. Specifically, claims 17 and 18 recite the position of the p53 mutation and patient outcome, and claims 19 and 20 recite the position of the p53 mutation and whether the patient is node negative or positive.

Summary

Applicants respectfully submit that the above remarks and/or amendments fully address and overcome the outstanding rejections. For the foregoing reasons, Applicants respectfully request the Examiner to withdraw all of the outstanding rejections and objections, and to issue a Notice of Allowance indicating the patentability of the present claims. Early and favorable action of the merits of the present application is thereby respectfully requested.

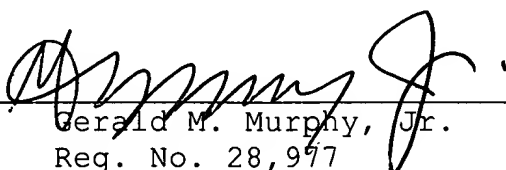
Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Kristi L. Rupert, Ph.D. (Reg. No. 45,702) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of three (3) months to September 23, 2004, in which to file a reply to the Office Action. The required fee of \$950.00 is attached to the Notice of Appeal, which is being filed concurrently herewith.


If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,
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